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How do pain and function vary with compartmental distribution and severity of radiographic knee osteoarthritis?

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Objectives. In radiographic OA (ROA) of the knee, how does radiographic severity and pattern of compartmental involvement influence symptoms?
Methods. Population-based study of 819 adults aged ≥50 yrs with knee pain. The severity of knee pain and function were measured using the Western Ontario and McMaster Universities scale. Three radiographic views of the knees were obtained.
Results. Seven hundred and seventy-seven participants were eligible (mean age 65.5 yrs, 357 males). Higher ROA severity in each of the tibiofemoral (TF) and patellofemoral (PF) compartments was independently associated with higher mean pain scores (TF: $F_{2,700} = 9.0$, $P < 0.0001$, PF: $F_{2,700} = 12.7$, $P < 0.0001$). The same pattern was found for mean function scores (TF: $F_{2,705} = 7.1$, $P = 0.001$, PF: $F_{2,705} = 15.9$, $P < 0.0001$). If either the TF or PF compartment was affected by moderate/severe OA, the added presence of OA in the other compartment did not increase the mean pain or function scores.
Conclusions. It is the severity of radiographic disease within a compartment, rather than the distribution of radiographic disease between compartments that is associated with symptoms. ROA in the PF joint is associated with symptoms, emphasizing the importance of radiographic changes in his joint.

Key words: Knee osteoarthritis, Pain, Function, Clinical Assessment Study of the Knee, Radiographic severity, Population study.

Introduction

The relationship between radiographic OA (ROA) and symptoms continues to be debated. In a recent population study, we reported a consistent cross-sectional relationship between increasing symptoms and the presence of ROA in a group of individuals with knee pain, when ROA and symptoms were characterized in detail [1]. Having established this relationship, further investigation is warranted to establish if the degree of ROA is directly related to increasing symptom severity.

The association between the degree of ROA and the presence of knee pain has been previously demonstrated in population studies [2–9], as has an association between ROA and disability [10]. However, this has not been consistent across all population studies [8, 11].

Population studies have frequently limited radiographic data collection to the tibiofemoral (TF) joint, but establishing whether specific compartmental patterns of ROA are associated with different symptoms is important. An association between patellofemoral (PF) OA and pain [9, 12, 13] and disability [12] has been reported. Szebenyi *et al*. [14] studied the involvement of different compartments (i.e. TF or PF) on symptoms and suggested that knees with structural damage in both compartments were more likely to be painful and associated with loss of function, compared with solitary compartmental disease. However, symptomatic unicompartmental OA is common [15]; hence, not only should compartmental involvement be studied but also the level of radiographic severity within that compartment if the true structure–symptom relationship is to be determined.

In order to specifically address the question of symptoms associated with different radiographic patterns, we have specifically studied the relationship between symptom severity and both (i) the degree of ROA and (ii) the compartmental distribution of ROA, using extended radiographic views and detailed symptom questioning.

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Methods

The Clinical Assessment Study of the Knee [CAS(K)] is a prospective observational cohort study of people with knee pain, sampled from the general population. All patients aged ≥50 yrs registered with three general practices in North Staffordshire, UK, were invited to take part in a two-stage postal survey. Almost all patients in the United Kingdom are registered with a general practitioner, and local registers provide a convenient sampling framework for the open population irrespective of any consultation they have had. Respondents to this survey phase, who indicated that they had experienced knee pain within the previous 12 months, were invited to attend a research clinic for a detailed assessment. This consisted of clinical interview, physical examination, digital photography, plain radiographs, anthropometric measurement and a brief self-complete questionnaire. Detailed descriptions of the study [16], and recruitment and retention of participants [17] have been previously published.

This article reports on cross-sectional analyses of baseline data from the CAS(K) study. Participants with complete radiographic data were included in this analysis. Ethical approval was obtained from the North Staffordshire LREC, No 1430, for all phases of the study and all participants provided written consent.

Data collection

Clinical data. Data on the severity of knee pain and function was gathered by self-complete questionnaire. The 24-item Western Ontario and McMaster Universities (WOMAC) OA index Likert version 3.0 [18, 19] was used. Each item has five response options (none, mild, moderate, severe, extreme) and yielded total subscale scores for pain (5 items, total score 0–20) and function (17 items, total score 0–68). BMI was calculated from weight and height measured at the assessment clinic.

Radiographic views. Three views of the knee were obtained: a weight-bearing posteroanterior (PA) semi-flexed/metatarsophalangeal view according to the Buckland-Wright protocol [20], a skyline and a lateral view. Skyline and lateral views were obtained with the participants in a supine position, the knee flexed to 45° using a wedge for accuracy. Films were obtained in the radiology department at the local University Hospital NHS Trust, by a team

of six radiographers who had undergone training to standardize the X-rays and who met for regular quality control sessions.

Radiographic scoring. A single reader (R.D.) scored all study films blinded to all clinical and questionnaire data. Intraobserver and interobserver repeatability was assessed in 50 participants (100 knees); the second reader for the interobserver assessment (P.C.) had previous experience of grading knee radiographs. Unweighted κ-coefficients were calculated. Intraobserver reliability scores for the PA Kellgren and Lawrence (K&L) score, skyline K&L score and lateral osteophytes were very good (unweighted $\kappa = 0.81$–0.98); interobserver scores were good ($\kappa = 0.49$–0.76).

The TF joint was assessed using the PA view and the posterior compartment of the lateral view. The PF joint was assessed using the skyline and lateral views. On the basis of the authors' original written description, a K&L grade was assigned to both the PA and skyline views [21]. In the lateral view, superior and inferior patellar osteophytes were scored using a standard atlas [22]. Osteophytes on the posterior tibial surface do not appear in the atlas but were judged on a similar basis of severity as other osteophytes in the lateral view. Detailed results of the repeatability, radiographic scoring and definitions have been previously published [15].

Radiographic severity of the TF and PF compartments was defined as mild or moderate/severe according to Table 1. Nine radiographic subgroups were used to analyse the association between ROA and symptoms (Table 2).

Statistical analysis

Only one knee per individual was analysed, the 'index knee'. In participants with unilateral knee pain, the index knee was this single painful knee. In those with bilateral knee pain, the most painful knee was the index knee. In situations where participants thought that both knees were similarly painful, the index knee was selected at random.

Analysis of variance (ANOVA) was used to identify heterogeneity of the mean overall WOMAC pain and function scores between the radiographic subgroups, adjusting for age (age 50–59/60–69/70–79/80 + yrs), gender and BMI (BMI $\leq$ 24.9/25–29.2/$\geq$30 kg/m^2). The *F*- and *P*-values are quoted and the presence of a linear trend explored. An independent two-sample *t*-test was applied when means between two groups were compared.

TABLE 1. Radiographic severity

	Normal	Mild	Moderate/severe
TF OA	PA K&L = 0 or 1 AND Posterior osteophytes = 0	PA K&L = 2 OR Posterior osteophytes = 1 or 2	PA K&L $\geq$ 3 OR Posterior osteophytes = 3
PF OA	Skyline K&L = 0 or 1 AND Lateral osteophytes = 0	Skyline K&L = 2 OR Lateral osteophytes = 1 or 2	Skyline K&L $\geq$ 3 OR Lateral osteophytes = 3

TABLE 2. Number of individuals in each radiographic subgroup (percentages in brackets)

Radiographic subgroup	Number in group (%)
Normal radiographs	246 (32)
Isolated OA: mild TF	22 (3)
Isolated OA: moderate/severe TF	9 (1)
Isolated OA: mild PF	142 (18)
Isolated OA: moderate/severe PF	44 (6)
Combined OA: mild TF and mild PF	60 (8)
Combined OA: mild TF and moderate/severe PF	60 (8)
Combined OA: moderate/severe TF and mild PF	121 (15)
Combined OA: moderate/severe TF and moderate/severe PF	73 (9)

Results

Participants

Over a 14-month period 819 people attended the research clinic, of whom 777 were eligible for current analysis (420 females and 357 males; mean (S.D.) age 65.5 (8.7) yrs; BMI (S.D.) 29.6 (5.2) kg/m^2). Reasons for ineligibility were: patient-declined radiography (2), incomplete radiographic data [total knee replacement in index knee (15), unlabelled PA views (2), absent patella (2) and skyline views deemed uninterpretable (5)] and existing diagnosis of inflammatory arthritis, verified by medical record review (16).

In all, 531 (68%) participants from the study sample were classified as having radiographic OA, moderate/severe OA being present in 307 participants. The distribution of individuals across the nine radiographic subgroups is shown in Table 2.

Association between pain and ROA

Radiographic severity. Radiographic severity was associated with increasing mean WOMAC pain scores. For OA of the 'whole' knee there was heterogeneity of pain scores between normal, mild and moderate/severe radiographic groups, $F_{2,700} = 13.8$, $P < 0.0001$, the association being strongly linear. When TF and PF OA were separately analysed, similar trends of increasing pain scores with radiographic severity were also seen; $F_{2,700} = 9.0$, $P < 0.0001$ and $F_{2,700} = 12.7$, $P < 0.0001$, respectively (Table 3).

Compartmental distribution. Variation in mean WOMAC pain score occurred across the nine radiographic subgroups (Fig. 1).

No heterogeneity existed between the five groups if moderate/severe ROA was present in one or more compartments ($F_{4,280} = 0.97$, $P = 0.422$). Further analysis showed that the presence of moderate/severe disease in both compartments was not associated with a higher pain score than moderate/severe disease in one compartment ($t = 1.784$, $P = 0.075$). It appears that

TABLE 3. Adjusted mean overall WOMAC pain scores for radiographic severity

	Normal	Mild ROA	Moderate/severe ROA	ANOVA
OA 'whole' knee				
N[a]	218	208	285	$F_{2,700} = 13.8$
WOMAC pain score[b]	5.17	5.83	7.28	$P < 0.0001$
TF OA				
N	392	128	191	$F_{2,700} = 9.0$
WOMAC pain score	5.75	6.09	7.42	$P < 0.0001$
PF OA				
N	246	300	165	$F_{2,700} = 12.7$
WOMAC pain score	5.16	6.54	7.35	$P < 0.0001$

[a]Due to missing WOMAC data *N* will vary. [b]Adjusted for age, gender and BMI *N* = number in the group

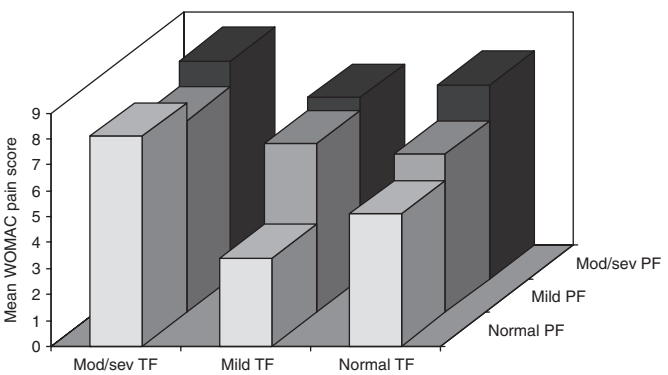

FIG. 1. Mean overall WOMAC pain score by radiographic subgroup.

a threshold in pain is reached once moderate/severe radiographic change is present in either the TF or PF compartment, and the addition of a second severe compartment does not alter the mean WOMAC pain score.

In the three groups where only mild ROA occurred, there was heterogeneity between the mean WOMAC pain score ($F_{2,205} = 3.6$, $P = 0.029$). Participants with mild isolated PF OA had a baseline pain score of 6.10 compared with 3.39 for mild isolated TF OA.

Associations between function and ROA

Radiographic severity. Table 4 shows the relationship between ROA and functional limitation to be a similar pattern to that of pain, mean function scores increasing with radiographic severity for the 'whole' knee and when the TF and PF compartments were analysed separately.

Compartmental distribution. Mean WOMAC function scores varied across the nine radiographic subgroups, the highest score occurring in the radiographic subgroup of isolated severe TF OA (Fig. 2). Analysis of the five radiographic subgroups where moderate/severe radiographic OA occurred in either one or both compartments revealed no heterogeneity ($F_{4,281} = 0.9$, $P = 0.86$). The presence of moderate/severe radiographic OA in both compartments was not associated with a higher mean WOMAC function score than moderate/severe disease in a single compartment ($t = -1.398$, $P = 0.163$). It appears, as with pain, that a threshold effect for function limitation is reached when moderate/severe radiographic change is present in either of the compartments and the addition of a second compartment with moderate/severe ROA does not alter the function score.

In participants with mild radiographic OA only, heterogeneity was demonstrated between the mean WOMAC function score for the three mild groups ($F_{2,207} = 4.9$, $P = 0.008$). Participants with mild isolated PF OA had a baseline function score of 20.3 compared with 10.0 for mild isolated TF OA.

TABLE 4. Adjusted mean overall WOMAC function scores for radiographic severity

	Normal	Mild ROA	Moderate/severe ROA	ANOVA
OA 'whole' knee				
N[a]	220	210	286	$F_{2,705} = 14.9$
WOMAC function score[b]	16.16	19.77	23.95	$P < 0.0001$
TF OA				
N	395	130	191	$F_{2,705} = 7.1$
WOMAC score	18.71	20.95	23.89	$P = 0.001$
PF OA				
N	248	304	164	$F_{2,705} = 15.9$
WOMAC score	16.20	21.73	24.51	$P < 0.0001$

[a]Due to missing WOMAC data *N* will vary. [b]Adjusted for age, gender and BMI. *N* = number in the group.

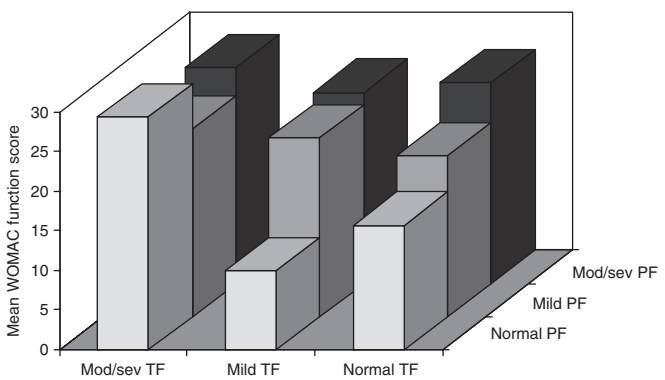

FIG. 2. Mean overall WOMAC function score by radiographic subgroup.

Discussion

Previous research within the CAS(K) cohort has demonstrated a relationship between symptom severity and the presence of ROA [1]. We have now extended this further, reporting that in a group of older people with knee pain, both radiographic severity and compartmental distribution of ROA are significantly associated with symptom and functional severity.

First, we have reported a relationship between the degree of radiographic change and the severity of knee pain and functional limitation. Previous studies have shown that knee pain is more likely to be present as radiographic severity increases [2–9] but these studies dichotomized knee pain as present or absent. We have provided further support to the relationship by demonstrating that radiographic severity is associated with increasing pain and functional limitation, this linear relationship occurring in OA of the whole knee joint but also when the TF and PF OA were studied separately. McAlindon *et al*. [10] reported an increase in frequency of disability with worsening ROA, and our results reinforce his observed relationship in both the TF and PF compartments. We have not adjusted for pain in our analysis of disability as we do not believe it to be a true confounder, but instead it lies on the causal pathway.

Second, although radiographic severity is important, the compartmental distribution may also influence symptom reporting, and our analysis has shown that a simple classification of pain and function levels is associated with different patterns of compartmental OA. Identifying whether ROA occurring in one compartment results in higher pain or function levels than in the other is a question of practical importance because of its implications for diagnosis and treatment. A further question is that if both compartments are affected, then is that additionally linked with pain and function? We found that for moderate/severe ROA there was no differentiation in pain or function score if moderate/severe ROA occurred alone or in combination with another compartment. This suggests that severity is more important than compartmental involvement. These results are in contrast with the study reported by Szebenyi *et al*. [14], who found that the presence of ROA in both the TF and PF compartments resulted in significantly higher pain and function scores. However, in this study radiographic severity was not considered and we know from previous work within the CAS(K) study (data not shown) that when TF or PF occur in isolation the disease is milder than when TF or PF OA occur in combined TF/PF OA. Szebenyi *et al*.'s results may reflect underlying severity of ROA rather than true compartmental involvement. In marked contrast to the CAS(K) study, Szebenyi *et al*. [14] found isolated TF and PF OA to be no more symptomatic than in persons with normal knee radiographs.

When our analysis was restricted to mild radiographic disease, heterogeneity existed between the three groups. In mild radiographic disease, isolated mild PF OA appears to be associated with higher pain and function scores compared with isolated mild TF OA in our population study. However, caution needs to be exercised in our cohort because of small numbers in the group with isolated TF OA ($n = 22$).

Third, we report a high prevalence of PF OA in our cohort, 24% of individuals demonstrating isolated PF disease. Previously, McAlindon highlighted the importance of the PF joint and a recent editorial reemphasized this importance [12, 23] and our results support this. Notably, we found that even isolated mild PF OA resulted in significant symptoms and this warrants further investigation particularly with regard to everyday task-specific functions. These findings may be relevant to orthopaedic surgeons when deciding between a unicompartmental and total knee replacement.

A total of 3106 adults aged ≥50 yrs reporting knee pain in the previous 12 months were identified from the first baseline questionnaire, of which 819 attended the research clinic.

There was evidence of selective non-participation during recruitment (aged ≥80 yrs, lower socioeconomic group, currently in employment, experiencing anxiety or depression, brief episode of knee pain in the previous year). This did not cause significant bias in either the distribution of WOMAC scores or the association between physical function and obesity. Our current analysis adjusted for age, gender and BMI, and we feel that the selective non-participation during recruitment will not substantially bias our estimates of the association between symptoms and radiographs.

The CAS(K) study did not sample asymptomatic individuals, and we cannot therefore state how much ROA would be present in individuals with no knee pain. However, it is the observed association between the severity of radiographic knee OA and increasing pain and functional limitation that is the main contribution of this article. Another limitation is the small number of individuals with isolated TF OA. Comparisons regarding pain and function levels with symptomatic participants with normal radiographs and isolated TF OA may be biased due to the small numbers.

The particular strengths of the CAS(K) study are (i) a clearly defined population, (ii) more radiographic views than in many previous studies and detailed scoring of the X-rays and (iii) detailed accounts of pain and function; thus increasing the likelihood of demonstrating associations if they exist.

This work implies that unicompartmental progression of knee OA does have consequences for symptoms and function. One particular pattern of progression that may have been underappreciated is progression of disease within the PF compartment. Further research is warranted on what effect conservative treatment may have on disease progression within this joint compartment. Our findings are cross-sectional and further longitudinal research would usefully identify the rate of PF progression and its associations with change in pain and function.

In conclusion, the results reported in this article suggest that structure is still likely to have an important role to play in the prevention of onset and progression of OA, as well as general risk factors for chronic pain and disability in an ageing population.

Rheumatology key messages

- Radiographic severity is significantly associated with severity of pain and function at the knee.
- Moderate/severe OA in any single compartment of the knee is as strong a determinant of symptoms as multi-compartment disease.

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